201-14217

[illegible] Mongan "Edwin L. [illegible] mongan-e@[illegible]" [illegible] 12:46:56 PM

To: oppt.ncic@epamail.epa.gov, Rtk Chem/DC/USEPA/US@EPA
cc: Georgia R Pugh <Georgia.R.Pugh@usa.dupont.com>, Jim_Keith@americanchemistry.com

Subject: Corfree(R) M1 HPV Robust Summary/Test Plan Submittal

Dear Sir or Madam,

Attached to this message is a .pdf file containing a cover letter, a Robust Data Summary and a Test Plan for the chemical Corfree(R) M1, also known as Reaction Product (Cyclododecanol /Cyclododecanone /Nitric Acid), High-Boiling Fraction, CAS# 72162-23-3, for the HPV Challenge Program. Please post this information on the EPA HPV Challenge website. I have also attached a word version of the cover letter in addition to the signed copy of the cover letter in the .pdf file.

Regards,

Edwin L. Mongan
Manager, Environmental Stewardship
DuPont Company
(See attached file: corfree m1 robust summary 12-30-02.PDF)(See attached file: corfree cover letter 12-30-02.doc)


corfree m1 robust summary 12-30-02.PDF


corfree cover letter 12-30-02.doc

Safety, Health & Environment Excellence Center
1007 Market Street, DuPont 6082
Wilmington, DE 19898
302-773-0910 (Office) – 302-774-3140 (Fax)

December 19, 2002

Christine Todd Whitman, Administrator
U.S. Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 2216

Attn: Chemical Right-to-Know Program

Dear Administrator Whitman,

E. I. du Pont de Nemours & Company, Inc. is pleased to submit the proposed test plan along with the robust summary for the chemical, Reaction Product (Cyclododecanol /Cyclododecanone /Nitric Acid), High-Boiling Fraction, CAS# 72162-23-3. Du Pont understands there will be a 120-day review period for the test plan and that all comments received by the EPA will be forwarded to DuPont for consideration.

This submission includes one electronic copy in .pdf format.

Please feel free to contact me with any questions or concerns you may have with regards to this submission at Edwin.L.Mongan-1@usa.dupont.com or by phone at 302-773-0910.

Sincerely,

Edwin L. Mongan, III
Manager, Environmental Stewardship
DuPont Safety, Health & Environment

Cc: Charles Auer – U.S. EPA
Office of Pollution Prevention & Toxics
U. S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

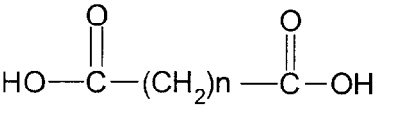
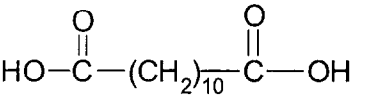
201-14217A

December 19, 2002

ROBUST SUMMARY FOR CORFREE® M1

Summary

Corfree® M1 is a mixture of dibasic acids, primarily dodecanedioic acid (DDDA) (~38-49%) and undecanedioic acid (~31-38%). The mixture also includes sebacic acid (~5-7%), other dibasic acids (~9-19%), other organics (~7-11%), nitrogen (~0.5%), and water (~0.3%). Available data are presented in this document on Corfree® M1 as well as DDDA (the largest component of the mixture). DDDA is not in the HPV program as it has previously been submitted under the Organisation for Economic Co-operation and Development (OECD) Screening Information Data Set (SIDS) Program (IPCS, n.d.); however, data will be presented on DDDA as it is the largest component in the Corfree® M1 mixture. A search of available toxicology data for undecanedioic acid (the second largest component of the mixture) did not produce any information.

Chemical Name	CAS Registry Number	Structure
Reaction product (cyclododecanol/ cyclododecanone/nitric acid) high-boiling fraction [referred to in document as Corfree® M1]	72162-23-3	 n=8-10
Dodecanedioic acid	693-23-2	

Scientific literature was searched and summarized (Table 1). Each study on these materials was evaluated for adequacy. Robust summaries were developed for each study addressing specific SIDS endpoints. Summaries were also developed for studies either considered not adequate but provided information of relevance for hazard identification and evaluation, or covered non-SIDS endpoints (Appendices A and B).

Table 1: Matrix of Available and Adequate Data on Corfree® M1 and DDDA

	Corfree® M1	DDDA
PHYSICAL/CHEMICAL CHARACTERISTICS		
Melting Point	√	√
Boiling Point	N/A	√
Vapor Pressure	√	√
Partition Coefficient	–/*	√
Water Solubility	–/*	√
ENVIRONMENTAL FATE		
Photodegradation	√	√
Stability in Water	√	√
Transport (Fugacity)	–/*	√
Biodegradation	√	√
ECOTOXICITY		
Acute Toxicity to Fish	–/*	√
Acute Toxicity to Invertebrates	√	√
Acute Toxicity to Aquatic Plants	–/*	√
MAMMALIAN TOXICITY		
Acute Toxicity	√	√
Repeated Dose Toxicity	–/*	√
Developmental Toxicity	–/*	√
Reproductive Toxicity	–/*	√
Genetic Toxicity Gene Mutations	√	√
Genetic Toxicity Chromosomal Aberrations	–/*	√/*

√ = Data are available and considered adequate.
√/* = No clastogenicity studies were available; however, an *in vivo* micronucleus study is available and will cover this endpoint.
–/* = No studies were available; however, results similar to DDDA are expected.
N/A = Not Applicable

Evaluation of Data Matrix Patterns

The available adequate data were broken out by discipline (physical/chemical, environmental fate, ecotoxicology, and mammalian toxicology). These comparisons were conducted to determine if a pattern existed among the materials and to determine if additional testing needed to be conducted to complete the data set for Corfree® M1.

Corfree® M1 and DDDA have roughly equivalent physical/chemical properties as a result of structural similarity. Complete and adequate data (Table 2) correlate well with structure and

validate the proposal to use the DDDA dataset to evaluate the toxicity of Corfree® M1. Corfree® M1 is a flaked solid with an average molecular weight of 215. Corfree® M1 softens at 85-95°C, has a flash point of 190°C, specific gravity of 1.02, and negligible vapor pressure at 25°C. DDDA is also a flaked solid and has a molecular weight of 230. DDDA melts at ca. 128°C, has a flash point of 220°C, specific gravity of 1.15, and vapor pressure of 21 mm Hg at 222°C.

Table 2: Physical and Chemical Characteristics

	Corfree® M1	DDDA
Physical Appearance	Solid white odorless flakes	Solid white odorless flakes
Molecular Weight	215	230.31
Water Solubility	No Data	30 mg/L @ 23°C
Melting Point	85-95°C (softens)	ca. 128°C
Boiling Point	Not applicable	250°C @ 48 mm Hg
Vapor Pressure	Negligible @ 25°C	21 mm Hg @ 222°C
Density/ Specific Gravity	1.02	1.15
Partition Coefficient (Log Kow)	No Data	3.18

DDDA is readily biodegradable. Additional environmental fate data for DDDA are generally not available. A review of estimated physical/chemical properties and environmental-fate characteristics based on output from EPIWIN 3.05 modeling software (Syracuse Research Corporation) indicates that it is unlikely to represent a hazard as a persistent and/or bioaccumulative chemical. When modeled using a Level III fugacity model under a standard scenario of equal emissions to air, water, and soil, DDDA is expected to partition primarily into soil and water compartments. At environmental pH, DDDA will be mostly in an ionized form when dissolved in water. Hydrolytic decomposition is not expected to readily transform DDDA, but it may be subject to photodegradation.

Data on environmental fate are generally not available for Corfree® M1. As a mixture, Corfree® M1 cannot be modeled for environmental fate characteristics. The reported components of the mixture were modeled individually. A review of estimated physical/chemical properties and environmental-fate characteristics based on output from EPIWIN 3.05 modeling software (Syracuse Research Corporation) indicates that the reported products in the Corfree® M1 mixture are unlikely to represent a hazard as persistent and/or bioaccumulative chemicals. The components are expected to generally behave in a manner similar to the C12 component, DDDA. Experimental data on biodegradation of Corfree® M1 show that it is

biodegradable, but did not qualify as readily biodegradable. Biodegradation test results for a mixture are difficult to interpret. The overall slower rate of degradation may indicate that one or more components had a degradation rate slower than that of DDDA. Alternatively, the well known diauxic growth phenomenon (Brock et al., 1984) causes sequential degradation starting with the most preferred substrate. Sequential utilization in a mixture can result in the total biodegradation of carbon in the mixture occurring at a slower rate that the rate for any one component.

Since the individual components of Corfree® M1 do not pose an environmental fate risk, Corfree® M1 should not pose an environmental fate risk and no environmental fate testing is recommended for Corfree® M1.

Table 3: Environmental Fate

	Corfree® M1	**DDDA**
Bioaccumulation*	No Data	BCF = 3.16
Biodegradation	Not readily biodegradable	Readily biodegradable
Fugacity*	No Data	Air 0% Water 18.5% Soil 81.1% Sediments 0.31%
* = Modeled data		

Modeling of physical/chemical parameters (i.e., Kow) and aquatic toxicity was conducted to help provide insight into the behavior in the environment and the aquatic toxicity of DDDA. Syracuse Research Corporation models for estimating physical/chemical properties were used to estimate $\log_{10}$ Kow (Meylan and Howard, 1995) for subsequent use in the ECOSAR program (Table 1). ECOSAR (Meylan and Howard, 1999) was used to estimate aquatic toxicity data for DDDA to green algae, daphnids (planktonic freshwater crustaceans), and fish. ECOSAR predictions are based on actual toxicity test data for classes of compounds with similar modes of action.

The existing test data, coupled with ECOSAR predictions, indicate that Corfree® M1 is unlikely to be acutely toxic to algae, invertebrates, or fish at environmentally relevant concentrations. The existence of both Corfree® M1 and DDDA as solids at temperatures less than approximately 80°C supports the low concern for acute aquatic toxicity. The other dibasic acids contained in Corfree® M1 are predicted by ECOSAR to be even less toxic than DDDA.

Table 4: Ecotoxicology

	Corfree® M1	DDDA
Log Kow	No Data	3.18
Toxicity to Fish (LC_{50} value)	No Data	48-hour > 1000 mg/L*(N)** 96-hour = 136 mg/L (E)**
Toxicity to Invertebrates (EC_{50} value)	48-hour > 120 mg/L (N)	24-hour > 27.6 mg/L (N) 48-hour = 158 mg/L (E)**
Toxicity to Algae (EC_{50} value)	No Data	72-hour > 5.8 mg/L (N) 96-hour = 105 mg/L (E)**

E = estimated value, N = value based on nominal test concentrations
* Sodium salt of DDDA was tested.
** Greater than the water solubility.

Acute toxicity data indicate that the chemicals exhibit similar acute toxicity (Table 5). Both chemicals have similar acute oral toxicity with LD_{50}s of > 5000 mg/kg and > 3000 mg/kg for Corfree® M1 and DDDA, respectively. These values represent the highest levels tested in their respective acute oral studies. Dermal LD_{50}s for both chemicals were above the highest levels tested, 2000 mg/kg and 6000 mg/kg respectively for Corfree® M1 and DDDA. Corfree® M1 appears to be more irritating to the skin and eye than DDDA. In addition, DDDA is not a dermal sensitizer.

Table 5: Acute Mammalian Toxicity

	Corfree® M1	DDDA
Oral LD_{50}	> 5000 mg/kg	> 3000 mg/kg
Inhalation ALC (4-hour)	No Data	> 4.3 mg/L
Dermal LD_{50} (24-hour)	> 2000 mg/kg	> 6000 mg/kg
Dermal Irritation	Moderate irritant	Not an irritant
Eye Irritation	Moderate irritant	Mild irritant
Dermal Sensitization	No Data	Not a sensitizer

A summary of the available data on repeated dose, developmental, and reproductive toxicity is shown in Table 6. No data were available on Corfree® M1 for repeated dose toxicity, developmental toxicity, or reproductive toxicity. DDDA was tested in a combined repeat dose/reproductive developmental screening test in rats. Dose levels of 100, 500, and 1000 mg/kg were tested. No mortality was observed at any dose level. DDDA did not significantly affect overall body weight, body weight gains, food consumption, or food efficiency in male or female rats which received DDDA via gavage for approximately 50 days. Male rats in the 500 and 1000 mg/kg groups had decreased lymphocyte counts. These were not considered adverse effects of the test substance since no morphological alterations were observed in the spleen, there were no decreases in thymus weights, and normal serum globulin concentrations were present. There were no gross or microscopic changes noted that were attributable to the test substance. Some transient cases of hypoactivity were observed shortly after dosing in the 500 and 1000 mg/kg males and the 1000 mg/kg females. There were no significant differences with respect to reproductive performance in male or female rats. The no-observed-adverse effect level (NOAEL) for the repeat dose, developmental, and reproductive toxicity sections of the study was 1000 mg/kg.

Table 6: Repeated Dose, Developmental, and Reproductive Toxicity

	Corfree® M1	**DDDA**
Repeated Dose Toxicity (NOAEL)	No Data	1000 mg/kg
Developmental Toxicity (NOAEL)	No Data	1000 mg/kg Not a developmental toxin
Reproductive Toxicity (NOAEL)	No Data	1000 mg/kg Not a reproductive toxin

Genetic toxicity data are similar between the chemicals (Table 7). Neither Corfree® M1 nor DDDA were mutagenic in the bacterial reverse mutation assay using *Salmonella typhimurium*. No data were available on the clastogenicity of Corfree® M1; however, DDDA did not induce micronuclei in an *in vivo* mouse micronucleus test.

Table 7: Genetic Toxicity

	Corfree® M1	DDDA
Mutagenicity	Negative	Negatve
Clastogenicity	No Data	Negative (micronucleus study)

Overall, the toxicologic database for Corfree® M1 is somewhat limited, but the information available suggests a level of toxicity comparable to DDDA. The 2 chemicals are similar in chemical structure, physical/chemical characteristics, environmental fate, aquatic toxicity, and acute toxicity. Because of these similarities, it is reasonable to conclude that these materials

would behave similarly in the areas where data gaps are evident: ecotoxicity, repeated dose toxicity, developmental toxicity, reproductive toxicity, and clastogenicity.

Exposure Assessment for Corfree® M1

Corfree® M1 is produced at one DuPont facility. Corfree® M1 is a reaction product of the nitric acid oxidation of cyclododecanol/cyclododecanone and is a mixture of dibasic acids, primarily dodecanedioic acid and undecanedioic acid. Corfree® M1 is used as a chemical intermediate in the production of corrosion inhibitors for metalworking fluids, engine coolants, and industrial cleaners.

The potential for exposure is the greatest in the Flaking Bay Area. The site can have approximately 1100 personnel working (construction, contractor, and plant employees). The areas where the substance is manufactured will have 16 total operators during normal operations and 40 people during a shutdown or major construction activity.

The site has effective safety, health, and environmental practices and procedures in addition to engineering controls, environmental controls, and personal protective equipment to control exposure. Adequate safety equipment, such as safety showers, eyewash fountains, and washing facilities, are available in the event of an occupational exposure.

Individuals handling Corfree® M1 should not breathe vapor, mist, or dust and should avoid contact with eyes, skin, and clothing. DuPont practices Responsible Care and assesses the ability of potential customers to safely handle Corfree® M1 prior to commencing a commercial relationship. The Product Stewardship System works with customers to understand their applications and any issues associated with PPE (personal protective equipment), safety equipment (safety showers, eyewash stations, ventilation needs, etc.), storage concerns, disposal requirements, and MSDS questions.

Area and personal air monitoring has been conducted on Corfree® M1 using the NIOSH 0500 - Nuisance Dust - Total Dust and MIE pDR-100AN Personal Particulate Monitor methods. LOGAN (lognormal analysis) is a computerized statistical method for characterizing occupational exposures to chemicals, noise, and other environmental hazards. LOGAN uses sequential collection of data and makes decisions on the minimum amount of data. It helps make cost-effective, accurate decisions that ensure a healthy workplace. LOGAN uses inferential statistics to estimate the true workplace conditions, in the same way that public polling estimates opinions by sampling a representative percentage of the public. LOGAN is designed to limit the risk of employee occupational overexposure to less than 5%.

No specific exposure limits have been established for Corfree® M1. The Permissible Exposure Limit (PEL) for particulates (not otherwise regulated) is 15 mg/m^3, 8-hour TWA, total dust; 5 mg/m^3, 8-hour TWA, respirable dust. The DuPont Acceptable Exposure Limit (AEL) -Total particulate concentration for nuisance dusts should not exceed 10 mg/m^3. None of the samples taken suggest the probability of exposure in excess of the PEL for particulates.

December 19, 2002

EXPOSURE DATA

Area
C12 Plant Operation 16 Flaker Bay

Operators

People	No. of Results	Avg. of TWA (ppm)	Min. of Results (ppm)	Max. of Results (ppm)
16	6	<0.50 mg/m^3	<0.50 mg/m^3	<0.50 mg/m^3

References for the Summary:

Brock et al. (1984). Biology of Microorganisms, Prentice-Hall, Englewood Cliffs, NJ.

IPCS (n.d.). International Programme on Chemical Safety, SIDS Dossier for Dodecanedioic acid (http://www1.oecd.org/ehs/sidstable/index.htm accessed on November 12, 2002).

Meylan, W. M. and P. H. Howard (1995). J. Pharm. Sci., 84:83-92.

Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210 (submitted for publication).

December 19, 2002

TEST PLAN FOR CORFREE® M1

Corfree® M1 CAS No. 72162-23-3	Data Available	Data Acceptable	Testing Required
Study	**Y/N**	**Y/N**	**Y/N**
PHYSICAL/CHEMICAL CHARACTERISTICS			
Melting Point	Y	Y	N
Boiling Point	N/A	N/A	N
Vapor Pressure	Y	Y	N
Partition Coefficient	Y*	Y	N
Water Solubility	Y*	Y	N
ENVIRONMENTAL FATE			
Photodegradation	Y	Y	N
Stability in Water	Y	Y	N
Transport (Fugacity)	Y*	Y	N
Biodegradation	Y	Y	N
ECOTOXICITY			
Acute Toxicity to Fish	Y*	Y	N
Acute Toxicity to Invertebrates	Y	Y	N
Acute Toxicity to Aquatic Plants	Y*	Y	N
MAMMALIAN TOXICITY			
Acute Toxicity	Y	Y	N
Repeated Dose Toxicity	Y*	Y	N
Developmental Toxicity	Y*	Y	N
Reproductive Toxicity	Y*	Y	N
Genetic Toxicity Bacterial Gene Mutations	Y	Y	N
Genetic Toxicity Chromosomal Aberrations	Y*	Y	N

Y = Yes
N= No
N/A = Not applicable
Y* = Data available on the largest component of the mixture, DDDA.

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APPENDIX A

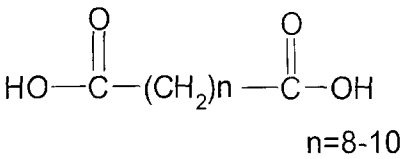
Existing published and unpublished data were collected and scientifically evaluated to determine the best possible study or studies to be summarized for each required endpoint. In the spirit of this voluntary program, other data of equal or lesser quality are not summarized, but are listed as related references at the end of each appropriate section, with a statement to reflect the reason why these studies were not summarized.

1.0 Substance Information

CAS Number: 72162-23-3

Chemical Name: Reaction product (cyclododecanol/cyclododecanone/nitric acid) high-boiling fraction

Structural Formula:



Other Names: Corfree® M1

Corfree® M1 - Nitric acid, reaction products with cyclododecanol and cyclododecanone, by-products from high-boiling fraction

Exposure Limits: No Data.

2.0 Physical/Chemical Properties

2.1 Melting Point:

Value:	85-95°C (softens)
Decomposition:	No Data
Sublimation:	No Data
Pressure:	No Data
Method:	No Data
GLP:	Unknown
Reference:	DuPont Co. (1996). Material Safety Data Sheet No. 6083CR (July 11).
Reliability:	Not assignable because limited study information was available.

Additional References for Melting Point: None Found.

2.2 **Boiling Point:** Not Applicable.

2.3 **Density**

Value:	1.02 (Specific gravity)
Temperature:	No Data
Method:	No Data
GLP:	Unknown
Results:	No additional data.
Reference:	DuPont Co. (1996). Material Safety Data Sheet No. 6083CR (July 11).
Reliability:	Not assignable because limited study information was available.

Additional References for Density: None Found.

2.4 **Vapor Pressure**

Value:	Negligible
Temperature:	25°C
Decomposition:	No Data
Method:	No Data
GLP:	Unknown
Reference:	DuPont Co. (1996). Material Safety Data Sheet No. 6083CR (July 11).
Reliability:	Not assignable because limited study information was available.

Additional References for Vapor Pressure: None Found.

2.5 **Partition Coefficient (log Kow):** No Data.

2.6 **Water Solubility:** No Data.

2.7 **Flash Point**

Value:	190°C
Method:	Closed Cup
GLP:	Unknown
Reference:	DuPont Co. (1996). Material Safety Data Sheet No. 6083CR (July 11).
Reliability:	Not assignable because limited study information was available.

Additional References for Flash Point: None Found.

2.8 **Flammability:** No Data.

3.0 Environmental Fate

3.1 Photodegradation:

Concentration:	No Data
Temperature:	No Data
Direct Photolysis:	The C7-C12 diacid components of Corfree® M1 may be susceptible to aqueous photolysis due to the presence of a C=O bond.
Indirect Photolysis:	No Data
Breakdown Products:	No Data
Method:	Inspection of chemical structure
GLP:	Not Applicable
Reference:	Judith C. Harris. (1990). "Rate of Aqueous Chapter 8 In W. J. Lyman et al. (eds.). Handbook of Chemical Property Estimation Methods, American Chemical Society, Washington, DC.
Reliability:	Estimate based on known qualitative structure-activity relationships.

Additional References for Photodegradation: None Found.

3.2 Stability in Water:

Concentration:	No Data
Half-life:	None of the reported components of Corfree M1® is expected to readily hydrolyze in water.
% Hydrolyzed:	No Data
Method:	Modeled. HYDROWIN, v. 1.67 module of EPIWIN v3.05 (Syracuse Research Corporation). HYDROWIN estimates aqueous hydrolysis rate constants for the following chemical classes: esters, carbamates, epoxides, halomethanes and selected alkyl halides. HYDROWIN estimates acid- and base-catalyzed rate constants; it does NOT estimate neutral hydrolysis rate constants. The prediction methodology was developed for the U.S. Environmental Protection Agency and is outlined in Mill et al., 1987.
GLP:	Not Applicable
Reference:	Mill, T. et al. (1987). "Environmental Fate and Exposure Studies Development of a PC-SAR for Hydrolysis: Esters, Alkyl Halides and Epoxides" EPA Contract No. 68-02-4254, SRI International Menlo Park, CA.
Reliability:	Estimated values based on an accepted model.

Additional References for Stability in Water: None Found.

3.3 **Transport (Fugacity):** No Data.

3.4 **Biodegradation**

Value:	Corfree® M1 (Nitrite Free) reached a maximum biodegradability of 63% by Day 28. The test substance was not readily biodegradable. The test substance was not inhibitory to microorganisms in the inoculum.
Breakdown Products:	Carbon Dioxide
Method:	The procedure used in the test were based on the recommendations of the following guidelines: OECD Guidelines for the Testing of Chemicals; Ready Biodegradability: 301B – CO_2 Evolution Test (1992). The test substance was tested for "Ready Biodegradability" using the 28-day Modified Sturm test. The biological system used was secondary activated sludge. At 0, 2, 4, 7, 10, 14, 21, and 28 days the carbon dioxide was trapped in barium hydroxide and was measured by titration of the residual hydroxide for inorganic carbon. The amount of CO_2 produced from the test substance was expressed as a percentage of the total CO_2 that the test material could have theoretically produced based on carbon composition ($ThCO_2$). If the measured CO_2 was greater than 60% of the ThOD or chemical oxygen demand (COD) within 28 days with the pass level being reached within 10 days after biodegradation exceeds 10%, then the test substance was classified as "ready biodegradable."
GLP:	Yes
Reference:	DuPont Co. (2002). Report No. EMSER 63-02, "Ready Biodegradability of Corfree® M1 (Nitrite Free) using the Modified Sturm Test (OECD 301B)" (October 29).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Biodegradation: None Found.

3.5 **Bioconcentration:** No Data.

4.0 Ecotoxicity

4.1 **Acute Toxicity to Fish:** No Data.

4.2 **Acute Toxicity to Invertebrates**

Type:	48-Hour EC_{50}
Species:	*Daphnia magna*
Value:	> 120 mg/L
Method:	The procedure used in the test were based on the recommendations of the following guidelines:

OECD Guideline 202.

European Economic Community 92/69 Annex V – Method C.2.

The acute toxicity to unfed *Daphnia magna* neonates, < 24 hours old at test start, was determined in an unaerated, 48-hour, static test. The study was conducted with 5 concentrations (7.5, 15, 30, 60, and 120 mg/L) and a dilution water control (originating from the Haskell Laboratory well). Four replicates with 5 daphnids per replicate were used per test substance concentration and control (20 daphnids per concentration).

Beakers (250 mL) were used as test chambers. Test chambers were covered with a glass plate during the test. Observations of test organisms were made daily. The criterion for the effect (immobility) was a lack of reaction to application of a gentle stimulus.

A recirculating water bath was used to maintain water temperature. A photoperiod of 16 hours light and 8 hours darkness was employed which included 30 minutes of transitional light preceding and following the 16-hour light period. Dissolved oxygen concentration, pH, total alkalinity, EDTA hardness, conductivity and temperature were measured in all replicates.

GLP:	Yes
Test Substance:	Corfree® M1 which consisted of:

42%	Dodecanedioic acid
31%	Undecanedioic acid

5%	Sebacic acid
11%	Other dibasic acids
10%	Monoacids and other organics
0.6%	Organic nitrogen compound

Results: Exposure of daphnids to nominal concentrations of 7.5, 15, 30, 60, and 120 mg/L resulted in 0, 5, 0, 0, and 0% immobility, respectively, at the end of 48 hours. No immobility was observed in the water control daphnids. The highest nominal concentration causing no immobility at test end was 120 mg/L. The lowest nominal concentration causing 100% immobility at test end was > 120 mg/L.

The nominal 7.5 mg/L test substance solution was clear with no color. The test solutions for the nominal concentrations of 15, 30, 60, and 120 mg/L were clear and colorless with small particles of undissolved test material observed.

Total alkalinity of the water control and 120 mg/L concentrations was 42 and 28 mg/L as $CaCO_3$, respectively. EDTA hardness of the water control and 120 mg/L concentrations was 131 and 130 mg/L as $CaCO_3$, respectively. Conductivity of the water control and 120 mg/L concentrations was 295 and 310 µmhos/cm, respectively.

The water chemistry characteristics of test solutions are presented in the following table.

Concentration (mg/L)	Temperature (°C)	Dissolved Oxygen (mg/L)	pH
0	20.2-20.6a 20.7-20.9	7.3-7.4a 8.5-8.7	7.8-7.9a 8.0
7.5	20.3-20.4a 20.7-20.8	7.3-7.5a 8.5-8.6	7.6-7.7a 7.9-8.0
15	20.3-20.4a 20.7-20.9	7.4-7.5a 8.6	7.5a 7.9
30	20.3-20.4a 20.8-20.9	7.4-7.5a 8.5	7.3a 7.7-7.8

60	20.3a 20.7-20.8	7.5a 8.6	7.2a 7.6
120	20.3-20.4a 20.7-20.9	7.6a 8.4-8.6	5.7-5.8a 6.0

a = Measurement at 0 hours. All other measurements were done at 48 hours.

Reference: DuPont Co. (2002). Unpublished Data, Haskell Laboratory Report DuPont-10699, "Static, Acute, 48-hour EC_{50} to *Daphnia magna*" (March 18).

Reliability: Medium because a study design was used with nominal concentrations only.

Additional References for Acute Toxicity to Invertebrates: None Found.

4.3 Acute Toxicity to Aquatic Plants: No Data.

5.0 Mammalian Toxicity

5.1 Acute Toxicity

Type: **Oral LD_{50}**
Species/Strain: Male and female rats/Crl:CD®(SD)IGS BR
Value: > 5000 mg/kg
Method: The procedures used in the test were based on the recommendations of the following guidelines:

U.S. EPA Pesticide Assessment Guidelines, Subdivision F, Section 81-1 (1984).

OECD Guidelines for the Testing of Chemicals, Section 4: Health Effects, No. 401 (1987).

Commision Directive 92/69/EEC, Annex V – Method B1 (1992).

Five male and 5 female rats (aged 57 and 78 days old, respectively) were intragastrically intubated at a single dose of 5000 mg/kg. Rats were fasted approximately 20.5 hours prior to dosing, with food being returned approximately 3 hours after dosing. The test substance was mixed with acetone prior to the addition of deionized water. Rats were dosed at a volume of approximately 16.67 mL per kg of body weight. The dosing mixture was stirred prior to and

throughout the dosing procedure.

Observations during the 15-day test period included mortality checks, body weight determinations, and observations for clinical signs of toxicity. On test day 15, the rats were euthanized and necropsied to detect grossly observable evidence of organ or tissue damage or dysfunction.

GLP: No

Test Substance: Corfree® M1 which consisted of:

Wt%	
46	Dodecanedioic acid
31	Undecanedioic acid
5	Sebacic acid
11	Other dibasic acids

Results: No deaths occurred during the study. No clinical signs of toxicity were observed in 4 female rats or 3 male rats. Lung noise was observed in 1 male rat on test day 2 only. Another male rat exhibited clinical signs from test day 13 until study completion. The signs observed in this rat included lethargy, bloated perineum, lung noise, red-stained face and paws, and ruffled fur. One female rat exhibited red-stained head on test day 3 only.

The male rat that exhibited delayed clinical signs lost approximately 5% of the body weight collected on test day 2 by day 3. By study completion, this rat also exhibited a cumulative body weight loss of approximately 29% of the body weight collected on day 8. No other significant body weight losses were observed in male rats. Body weight losses of 2 or 3% of previously determined body weight were observed sporadically in some female rats during the study.

No test substance-related gross lesions were observed at necropsy.

Reference: DuPont Co. (1999). Unpublished Data, Haskell Laboratory Report DuPont-2182, "Acute Oral Toxicity Study in Male and Female Rats" (March 18).

Reliability: High because a scientifically defensible or guideline method was used.

Additional References for Acute Oral Toxicity: None Found.

Type: **Acute Inhalation Toxicity:** No Data.

December 19, 2002

Type:	**Dermal LD_{50}**
Species/Strain:	Male and female New Zealand White rabbits/HM:(NZW)fBR
Exposure Time:	24 hours
Value:	> 2000 mg/kg
Method:	The procedures used in the test were based on the recommendations of the following guidelines: OECD Guidelines for the Testing of Chemicals, Section 4: Health Effects, No. 402 (1987). Commision Directive 92/69/EEC, Annex V – Method B3 (1992). A single dose of the test substance was applied to the shaved, intact skin of 5 male and 5 female young adult rabbits at a dosage of 2000 mg/kg. The application site was occluded for 24 hours, after which the test substance was removed. The rabbits' body weights ranged from 2123.8 to 2265.1 g for males and 2008.3 to 2089.7 g for females on the day of dosing. The animals were observed on the day of dosing and during a 14-day observation period. Observations during the 15-day test period included daily mortality checks, periodic body weight determinations, and daily observations for clinical signs of toxicity and dermal irritation (weekends excluded). The rabbits were necropsied to detect grossly observable evidence of organ or tissue damage or dysfunction at the end of the 15-day test period. Dermal effects were scored according to the Draize scale.
GLP:	No
Test Substance:	Corfree® M1 which consisted of: Wt% 46 Dodecanedioic acid 31 Undecanedioic acid 5 Sebacic acid 11 Other dibasic acids
Results:	No deaths, clinical signs of toxicity, or test substance-related body weight losses were observed during the study. Slight, mild, or moderate erythema was observed in treated rabbits the day the test substance was removed (test day 2);

no edema was observed. No erythema was observed past test day 6. Eight rabbits exhibited yellow-stained fur (last observed on day 13) and 3 rabbits exhibited desquamation (last observed on day 12).

Body weight losses of up to approximately 8% of initial body weight were observed on test day 2 in 8 rabbits. These weight losses were not considered to be test substance-related, but were attributed to stress associated with the wrapping procedure and/or to the rabbits wearing collars.

The gross observation of small right testis observed in 1 male rabbit was non-specific and not indicative of target organ toxicity.

Reference: DuPont Co. (1999). Unpublished Data, Haskell Laboratory Report DuPont-2603, "Acute Dermal Toxicity Study in Rabbits" (March 18).

Reliability: High because a scientifically defensible or guideline method was used.

Additional References for Acute Dermal Toxicity: None Found.

Type: **Dermal Irritation**

Species/Strain: Male and female New Zealand White rabbits/HM:(NZW)fBR

Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

One female and 5 male young adult rabbits were used in the test. One rabbit was treated dermally with the test substance 1 day prior to the other 5 rabbits to ensure the test substance was neither corrosive nor a severe skin irritant. The body weights of the rabbits ranged from 2396 to 3183 g on the day of treatment.

Approximately 0.5 g of the test substance was applied to the shaved, intact skin of each rabbit and covered with a semi-occlusive dressing for a 4-hour exposure. Approximately 1, 24, 48, and 72 hours after removal of the test substance, the test sites were evaluated for erythema, edema, and other evidence of dermal effects and were scored according to the Draize scale. The adjacent areas of untreated skin were used for comparison.

GLP: No

Test Substance:	Corfree® M1 which consisted of:
	Wt%
	46 Dodecanedioic acid
	31 Undecanedioic acid
	5 Sebacic acid
	11 Other dibasic acids
Results:	The test substance was a moderate skin irritant.
	The test substance stained the skin of 5 rabbits yellow; however, the test sites could still be evaluated for erythema. One rabbit exhibited no dermal irritation during the study. The test substance produced no to mild erythema by 1 and 24 hours after test substance removal. By 48 and 72 hours, all rabbits except 1 were clear of all irritation; the last rabbit exhibited moderate erythema. No edema, clinical signs of toxicity, or significant body weight losses were observed during the study.
Reference:	DuPont Co. (1999). Unpublished Data, Haskell Laboratory Report DuPont-2450, "Skin Irritation Test in Rabbits" (March 18).
Reliability:	High because a scientifically defensible or guideline method was used.
Type:	**Dermal Irritation**
Species/Strain:	Not Applicable
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.
	A membrane disk containing the biobarrier matrix was placed into a chemical detection system (CDS) vial. Approximately 0.5 grams of the test substance, ground with a mortar and pestle, was placed on the top of the disc. The vial was then observed for a change in the CDS. This procedure was followed for each of 4 test vials. Vial 5 was similarly treated with a positive control (sulfuric acid) and Vial 6 was similarly treated with a negative control (citric acid). Vials 1-4 were observed for > 240 minutes.
GLP:	No

Test Substance: Corfree® M1 which consisted of:

Wt%	
46	Dodecanedioic acid
31	Undecanedioic acid
5	Sebacic acid
11	Other dibasic acids

Results: The test substance did not pass through any of the membranes. The test substance was not a corrosive substance.

Reference: DuPont Co. (1999). Unpublished Data, Haskell Laboratory Report DuPont-2138, "Corrositex® *In Vitro* Test" (February 17).

Reliability: High because a scientifically defensible or guideline method was used.

Additional References for Dermal Irritation: None Found.

Type: **Dermal Sensitization:** No Data.

Type: **Eye Irritation**

Species/Strain: Male New Zealand White rabbits/HM:(NZW)fBR

Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

The test substance was tested for eye irritation potential in 2 young adult rabbits. The rabbits weighed 2778 or 3018 g on the day of treatment. The rabbits used on the study were free of pre-existing corneal or conjunctival injury or irritation and were judged to be in good health.

Approximately 0.01 g of the test substance was instilled into the lower conjunctival sac of the right eye of each rabbit. Approximately 20 seconds after instillation, the treated and control eyes of 1 rabbit were washed. The treated and control eyes of the remaining rabbit were not washed. The eye of the rabbits were examined on the day of treatment and on days 1, 2, 3, and 7 following treatment. At each of these observation periods, eyes were examined using illumination and magnification and scored for ocular reactions according to the Draize scale. Clinical signs of toxicity and body weights were periodically recorded.

GLP: No

Test Substance: Corfree® M1 which consisted of:

	Wt%
	46 Dodecanedioic acid
	31 Undecanedioic acid
	5 Sebacic acid
	11 Other dibasic acids
Results:	The test substance was a moderate eye irritant.
	The test substance produced moderate conjunctival redness and moderate discharge in both treated rabbit eyes. In addition, slight chemosis was observed in the treated unwashed eye, and mild chemosis and blistering on the conjunctiva and the nictitating membrane were observed in the eye washed after treatment. Both treated eyes were normal by 7 days after administration of the test substance.
	No clinical signs of toxicity or body weight losses were observed during the study.
Reference:	DuPont Co. (1999). Unpublished Data, Haskell Laboratory Report DuPont-2565, "Eye Irritation Test in Rabbits" (April 9).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Eye Irritation: None Found.

5.2 Repeated Dose Toxicity: No Data.

5.3 Developmental Toxicity: No Data.

5.4 Reproductive Toxicity: No Data.

5.5 Genetic Toxicity

Type:	***In vitro* Bacterial Reverse Mutation Assay**
Tester Strain:	*Salmonella typhimurium* TA98, TA100, TA1535, and TA1537 *Escherichia coli* strain WP2 *uvr*A
Exogenous Metabolic Activation:	With and without Aroclor®-induced rat liver S9
Exposure Concentrations:	Initial mutagenicity assay: 100, 333, 1000, 3333, 5000 µg/plate
	Independent repeat assay: 75, 200, 600, 1800, and

5000 µg/plate

Method: The procedures used in the test were based on the recommendations of the following guideline:

OECD Test Guideline No. 471.

A preliminary toxicity test was used to establish the dose range for the mutagenicity test. Vehicle (dimethyl sulfoxide) and 10 dose levels of the test substance (6.7, 10, 33, 67, 100, 333, 667, 1000, 3333, and 5000 µg/plate) were plated.

The mutagenic potential of the test substance was evaluated in the mutagenicity test, which consisted of an initial and an independent repeat assay. The test system was exposed to the test substance via the plate incorporation method originally described by Ames, B. N. et al. (1975). Mutat. Res., 31:347-364 and updated by Maron, D. M. and B. N. Ames (1983). Mutat. Res., 113:173-215.

For each trial, 3 replicates were plated for each tester strain in the presence and absence of the exogenous metabolic activation system at each test substance concentration.

Positive controls included the following: 2-aminoanthracene, 2-nitrofluorene, sodium azide, 9-aminoacridine, and methyl methanesulfonate.

Test substance dilutions were prepared immediately before use. S9 or a sham mix, tester strain, and vehicle or test substance were added to molten selective top agar (containing L-histidine, D-biotin, and L-tryptophan) at 45±2°C. After vortexing, the mixture was overlaid onto the surface of 25 mL minimal bottom agar. When plating the positive controls, the test substance aliquot was replaced by an aliquot of appropriate positive control. After the overlay had solidified, the plates were inverted and incubated for approximately 48 to 72 hours at 37±2°C. Plates that were not counted immediately were stored at 2-8°C until colony counting could be conducted.

Bacterial background lawns were evaluated for evidence of test substance toxicity and precipitation. Evidence of toxicity was scored relative to the vehicle control plate. Revertant colonies for a given tester strain and condition were counted either entirely by an automated colony counter or entirely by hand unless the test was the preliminary

toxicity test or the plates exhibited toxicity. Plates with sufficient test substance precipitate to interfere with automated colony counting were counted manually.

For the test substance to be classified as positive (mutagenic), it must have caused a dose-related increase in the mean revertants per plate of at least one tester strain with a minimum of 2 increasing concentrations of test substance. Data sets for strains TA1535 and TA1537 were judged positive if the increase in mean revertants at the peak of the dose response was equal to or greater than 3 times the mean vehicle control value. Data sets for strains TA98, TA100, and WP2 *uvr*A were judged positive if the increase in mean revertants at the peak of the dose response was equal to or greater than 2 times the mean vehicle control value.

GLP: Yes

Test Substance: Corfree® M1 which consisted of:

49% Dodecanedioic acid
32% Undecanedioic acid
13% Other dibasic acids
6% Monoacids and other organics

Results: Negative

Remarks: Neither precipitate nor toxicity were observed in the initial or independent repeat assay. No positive responses were observed for any tester strains in the presence or absence of S9 activation in either the initial mutagenicity or in the independent repeat assay.

Reference: DuPont Co. (2000). Unpublished Data, Haskell Laboratory Report DuPont-4554, "Bacterial Reverse Mutation Test with an Independent Repeat Assay" (March 18).

Reliability: High because a scientifically defensible or guideline method was used.

Additional References for ***In vitro*** **Bacterial Reverse Mutation Assay:** None Found.

Type: ***In vitro*** **Clastogenicity Studies:** No Data.

Type: ***In vivo*** **Genetic Toxicity Tests:** No Data.

APPENDIX B

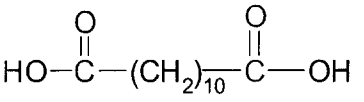
Existing published and unpublished data were collected and scientifically evaluated to determine the best possible study or studies to be summarized for each required endpoint. In the spirit of this voluntary program, other data of equal or lesser quality are not summarized, but are listed as related references at the end of each appropriate section, with a statement to reflect the reason why these studies were not summarized.

1.0 Substance Information

CAS Number: 693-23-2

Chemical Name: Dodecanedioic acid

Structural Formula:



Other Names:
1,10-Decanedicarboxylic acid
1,10-Dicarboxydecane
1,12-Dodecanedioic acid
C12 Dibasic acid
Corfree M2
Corfree M3
DDDA
Decamethylenedicarboxylic acid
n-Dodecanedioic acid
SL-AH

Exposure Limits: No Data

2.0 Physical/Chemical Properties

2.1 Melting Point

Value:	ca. 128°C
Decomposition:	No
Sublimation:	No
Pressure:	No Data
Method:	No Data
GLP:	No
Reference:	Huels AG (1993). Safety Data Sheet (October 4) (cited in IUCLID (2000). IUCLID Dataset, "Dodecandioic acid" (February 19)).
Reliability:	Not assignable because limited study information was available.

Additional References for Melting Point:

DuPont Co. (2000). Material Safety Data Sheet No. 6055CR (January 26).

Grasselli, J. G. and W. M. Ritchey (1975). Chemical Rubber Company Atlas of Spectral Data and Physical Constants for Organic Compounds, 2nd ed., CRC Press, Cleveland, Ohio (CIS/IS-0011820).

2.2 Boiling Point

Value:	250°C
Decomposition:	No Data
Pressure:	48 mm Hg
Method:	No Data
GLP:	No Data
Reference:	DuPont Co. (2000). Material Safety Data Sheet No. 6055CR (January 26).
Reliability:	Not assignable because limited study information was available.

Additional References for Boiling Point:

Huels AG (1993). Safety Data Sheet (October 4) (cited in IUCLID (2000). IUCLID Dataset, "Dodecandioic acid" (February 19)).

The 1977-78 Aldrich Catalog/Handbook of Organic and Biochemicals (1977). No. 18, Aldrich Chemical Co., Milwaukee, WI (CIS/IS-0011821).

SIDS Dossier for Dodecanedioic acid (http://www1.oecd.org/ehs/sidstable/index.htm accessed on November 12, 2002).

2.3 Density

Value:	1.15 (Specific gravity)
Temperature:	25°C
Method:	No Data
GLP:	Unknown
Results:	No additional data.
Reference:	DuPont Co. (2000). Material Safety Data Sheet No. 6055CR (January 26).
Reliability:	Not assignable because limited study information was available.

Value:	Density: 0.953 g/cm^3; Bulk density: ca. 600 kg/m^3
Temperature:	140°C
Method:	No Data
GLP:	No

Results:	No additional data.
Reference:	IUCLID (2000). IUCLID Dataset, 'Dodecandioic acid" (February 19)).
Reliability:	Not assignable because limited study information was available.

Additional References for Density: None Found.

2.4 Vapor Pressure

Value:	21 mm Hg
Temperature:	222°C
Decomposition:	No Data
Method:	No Data
GLP:	Unknown
Reference:	DuPont Co. (2000). Material Safety Data Sheet No. 6055CR (January 26).
Reliability:	Not assignable because limited study information was available.

Additional References for Vapor Pressure:

Huels AG (1993). Safety Data Sheet (October 4) (cited in IUCLID (2000). IUCLID Dataset, "Dodecandioic acid"(February 19)).

SIDS Dossier for Dodecanedioic acid (http://www1.oecd.org/ehs/sidstable/index.htm accessed on November 12, 2002).

2.5 Partition Coefficient (log Kow)

Value:	3.18
Temperature:	No Data
Method:	No Data
GLP:	Unknown
Reference:	Leo, A. J. (1982). Log P Values Calculated Using the CLOGP Program for Compounds in ISHOW Files, Pomona College Medicinal Chemistry Project, Seaver Chemistry Laboratory, Claremont, CA (CIS/IS-0011822).
Reliability:	Not assignable because limited study information was available.

Additional Reference for Partition Coefficient (log Kow):

Huels AG (n.d.). (cited in IUCLID (2000). IUCLID Dataset, "Dodecandioic acid" (February 19)).

2.6 Water Solubility

Value:	30 mg/L
Temperature:	23°C
pH/pKa:	No Data
Method:	No Data
GLP:	Unknown
Reference:	Kirk-Othmer Encyclopedia of Chemical Technology (1979). Vol. 7, 3rd ed., pp. 614-628, John Wiley & Sons, New York (cited in IUCLID (2000). IUCLID Dataset, "Dodecandioic acid" (February 19)).
Reliability:	Not assignable because limited study information was available.

Additional References for Water Solubility:

DuPont Co. (2000). Material Safety Data Sheet No. 6055CR (January 26).

Huels AG (1993). Safety Data Sheet (October 4) (cited in IUCLID (2000). IUCLID Dataset, "Dodecandioic acid" (February 19)).

Huels (1988). Unpublished Report No. ADW 170 (cited in IUCLID (2000). IUCLID Dataset, "Dodecandioic acid" (February 19)).

Huels (1988). Unpublished Report No. D-338 (cited in IUCLID (2000). IUCLID Dataset, "Dodecandioic acid" (February 19)).

2.7 Flash Point

Value:	220°C
Method:	Closed Cup, DIN51758
GLP:	No
Reference:	Huels AG (1993). Safety Data Sheet (October 4) (cited in IUCLID (2000). IUCLID Dataset, "Dodecandioic acid" (February 19)).
Reliability:	Not assignable because limited study information was available.

Additional Reference for Flash Point:

DuPont Co. (2000). Material Safety Data Sheet No. 6055CR (January 26).

2.8 Flammability

Results:	Ignition Temperature = 390°C
Method:	DIN 51794

GLP:	No Data
Reference:	Huels AG (1993). Safety Data Sheet (October 4) (cited in IUCLID (2000). IUCLID Dataset, "Dodecandioic acid" (February 19)).
Reliability:	Not assignable because limited study information was available.

Additional References for Flammability: None Found.

3.0 Environmental Fate

3.1 Photodegradation

Concentration:	No Data
Temperature:	No Data
Direct Photolysis:	DDDA may be susceptible to aqueous photolysis due to the presence of a C=O bond.
Indirect Photolysis:	No Data
Breakdown Products:	No Data
Method:	Inspection of chemical structure
GLP:	Not applicable.
Reference:	Judith C. Harris. (1990). Rate of Aqueous Photolysis. Chapter 8 In Lyman, W. J. et al. (eds.). Handbook of Chemical Property Estimation Methods, American Chemical Society, Washington, DC.
Reliability:	Estimate based on known qualitative structure-activity relationships.

Additional Reference for Photodegradation:

Atkinson, R. (1987). Int. J. Chem. Kinet., 19:799-828 (cited in IUCLID (2000). IUCLID Dataset, "Dodecandioic acid" (February 19)).

3.2 Stability in Water

Concentration:	No Data
Half-life:	Dodecanedioic acid is not expected to readily hydrolyze in water.
% Hydrolyzed:	No Data
Method:	Modeled. HYDROWIN, v. 1.67 module of EPIWIN v3.05 (Syracuse Research Corporation). HYDROWIN estimates aqueous hydrolysis rate constants for the following chemical classes: esters, carbamates, epoxides, halomethanes and selected alkyl halides. HYDROWIN estimates acid- and base-catalyzed rate constants; it does NOT estimate neutral

	hydrolysis rate constants. The prediction methodology was developed for the U.S. Environmental Protection Agency and is outlined in Mill et al., 1987.
GLP:	Not Applicable
Reference:	Mill, T. et al. (1987). "Environmental Fate and Exposure Studies Development of a PC-SAR for Hydrolysis: Esters, Alkyl Halides and Epoxides" EPA Contract No. 68-02-4254, SRI International, Menlo Park, CA.
Reliability:	Estimate based on an accepted model.

Additional References for Stability in Water: None Found.

3.3 Transport (Fugacity)

Media:	Air, water, soil, & sediments	
Distributions:	Air:	0%
	Water:	18.5%
	Soil:	81.1%
	Sediments:	0.31%
Half-life:	Air:	27.4 hour
	Water:	208 hour
	Soil:	416 hour
	Sediments:	1870 hour
Adsorption Coefficient:	Estimated Log Koc = 845.5	
Desorption:	Not Applicable	
Volatility:	Estimated Henry's Law Constant = 6.4340×10^{-12} atm-m3/mole; Group Method, 25°C	
Method:	Henry's Law Constant - HENRYWIN v. 3.10 module of EPIWIN v3.05 (Syracuse Research Corporation). Henry's Law Constant (HLC) is estimated by two separate methods that yield two separate estimates. The first method is the bond contribution method and the second is the group contribution method. The bond contribution method is able to estimate many more types of structures; however, the group method estimate is usually preferred (but not always) when all fragment values are available. Log Koc – Calculated from log Kow by the Mackay Level III fugacity model incorporated into EPIWIN v3.05 (Syracuse Research Corporation). Environmental Distribution - Mackay Level III fugacity model, in EPIWIN v3.05 (Syracuse Research Corporation). Emissions (1000 kg/hr) to air, water, and soil compartments.	
GLP:	Not Applicable	
Reference:	HENRYWIN - J. Hine and P. K. Mookerjee (1975). J. Org. Chem., 40(3):292-8; Meylan, W. and P. H. Howard (1991).	

	Environ. Toxicol. Chem., 10:1283-93. Fugacity - The methodology and programming for the Level III fugacity model incorporated into EPIWIN v3.05 (Syracuse Research Corporation) were developed by Dr. Donald MacKay and coworkers and are detailed in: Mackay, D. (1991). Multimedia Environmental Models: The Fugacity Approach, pp. 67-183, Lewis Publishers, CRC Press. Mackay, D. et al. (1996). Environ. Toxicol. Chem., 15(9):1618-1626. Mackay, D. et al. (1996). Environ. Toxicol. Chem., 15(9):1627-1637.
Reliability:	Estimated value based on an accepted model.

Additional References for Transport (Fugacity): None Found.

3.4 Biodegradation

Study No. 1

Value:	71% degraded after 28 days. Readily biodegradable.
Breakdown Products:	No Data
Method:	The procedures used in this test were based on the recommendations of the following guideline: OECD Guideline 301 D "Ready Biodegradability: Closed Test was aerobic. The inoculum was predominately domestic sewage.
GLP:	No
Reference:	Huels (n.d.). Unpublished investigation (cited in IUCLID (2000). IUCLID Dataset, "Dodecandioic acid" (February 19)).
Reliability:	High because a scientifically defensible or guideline method was used.

Study No. 2

Value:	94.4-98.8% degradation
Breakdown Products:	No Data
Method:	The procedures used in this test were based on the recommendations of the following guideline: OECD Guideline 303 A "Stimulation Test – Aerobic Sewage Treatment: Coupled Unit Test".

	Test was aerobic. The inoculum was activated sludge. Concentration was 10 mg/L related to DOC.
GLP:	No
Reference:	Huels (n.d.). Unpublished investigation (cited in IUCLID (2000). IUCLID Dataset, "Dodecandioic acid" (February 19)).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Biodegradation: None Found.

3.5 Bioconcentration

Value:	BCF = 3.16
Method:	Modeled. BCFWIN v. 2.4 module of EPINWIN v3.05 (Syracuse Research Corporation). BCFWIN estimates the bioconcentration factor (BCF) of an organic compound using the compound's log octanol-water partition coefficient (Kow) with correction factors based on molecular fragments.
GLP:	Not Applicable
Reference:	"Improved Method for Estimating Bioconcentration Factor (BCF) from Octanol-Water Partition Coefficient", SRC TR-97-006 (2nd Update), July 22, 1997; prepared for: Robert S. Boethling, EPA-OPPT, Washington, DC; Contract No. 68-D5-0012; prepared by: William M. Meylan, Philip H. Howard, Dallas Aronson, Heather Printup and Sybil Gouchie; Syracuse Research Corp.
Reliability:	Estimated value based on an accepted model.

Additional References for Bioconcentration: None Found.

4.0 Ecotoxicity

4.1 Acute Toxicity to Fish

Type:	**48-hour LC_{50}**
Species:	Golden orfe
Value:	> 1000 mg/L
Method:	The procedures used in the test were based on the recommendations of the following guideline: DIN 38412 Part 15. The sodium salt of dodecanedioic acid was tested in the acute fish test. The test species, Golden orfe, was tested

	over a period of 48 hours. Concentrations tested included 200, 500, and 1000 mg/L. No other details were presented.
GLP:	Yes
Test Substance:	The sodium salt of dodecanedioic acid, purity not reported
Results:	The maximum concentration tested with no effect was 1000 mg/L. No additional data were reported.
Reference:	Huels AG (1987). Biology - Toxicology, Report No. F705 (July 20).
Reliability:	Medium because a scientifically defensible or guideline method was used; however, limited study information was available.

From ECOSAR Model

Type:	**96-hour LC_{50}**
Species:	Freshwater fish
Value:	136 mg/L (greater than predicted water solubility)
Method:	Modeled, ECOSAR (using log Kow of 3.18)
GLP:	Not Applicable
Test Substance:	DDDA
Results:	No additional data.
Reference:	Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210 (submitted for publication).
Reliability:	Estimated value based on accepted model.

Additional Reference for Acute Toxicity to Fish: None Found.

4.2 Acute Toxicity to Invertebrates

Type:	**24-hour EC_{50}**
Species:	*Daphnia magna* (Strauss)
Value:	> 27.6 mg/L
Method:	The procedures used in the test were based on the recommendations of the following guideline: DIN 38412 Part 11. Dodecanedioic acid was tested with *Daphnia* for 24 hours. The test criterion was loss of swimming capability of the animals. From the dose-effect relationship, the concentration was calculated at which half of the animals had no further swimming ability. The concentration was

	measured by DOC content of saturated solution. No other details were presented.
GLP:	No
Test Substance:	Dodecanedioic acid, purity not reported
Results:	No toxic effect was observed up to a concentration of 26.7 mg/L. No additional data were reported.
Reference:	Huels AG (1988). Biology - Toxicology, Report No. D338 (July 27).
Reliability:	Medium because a scientifically defensible or guideline method was used; however, limited study information was available.

From ECOSAR Model

Type:	**48-hour EC_{50}**
Species:	Daphnid
Value:	158 mg/L (using log Kow of 3.18)
Method:	Modeled
GLP:	Not Applicable
Test Substance:	DDDA
Results:	No additional data.
Reference:	Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210 (submitted for publication).
Reliability:	Estimated value based on accepted model.

Additional References for Acute Toxicity to Invertebrates: None Found.

4.3 Acute Toxicity to Aquatic Plants

Study No. 1

Type:	72-hour growth rate NOEC
Species:	*Scenedesmus subspicatus*
Value:	> 5.8 mg/L
Method:	The procedure used in the test were based on the recommendations of the following guideline: Draft UBA proposal as of 2/1984. In an algae growth inhibition test, dodecanedioic acid was tested for ecotoxicological activity verses the algae *Scenedesmus subspicatus* for a duration of 72 hours.

	Inhibition of cell multiplication was measured as a function of substance concentration. From the dose-effect relationship, the concentration at which cell multiplication rate was reduced by half was calculated. The saturated solution contained 7.3 mg DOC/L.
	No other details were presented.
GLP:	No
Test Substance:	Dodecanedioic acid, purity not reported
Results:	No toxic effect was observed up to a concentration of 5.8 mg/L. No additional data were reported.
Reference:	Huels AG (1988). Biology - Toxicology, Report No. AW 170 (December 9).
Reliability:	Medium because a scientifically defensible or guideline method was used; however, limited study information was available.

Study No. 2

Type:	Assimilation Test
Species:	*Scenedesmus subspicatus*
Value:	> 15.3 mg/L
Method:	The procedures used in the test were based on the recommendations of the following guideline:
	Draft DIN 38412 Part 12.
	Inhibition of oxygen release as a function of substance concentration was measured. The dose-action relationship was used to calculate the concentration at which assimilation rate was reduced by half, and also for 10% inhibition. The test duration was 24 hours. The concentration was measured by DOC content of saturated solution.
	No other details were presented.
GLP:	Unknown
Test Substance:	Dodecanedioic acid, purity not reported
Results:	No toxic activity was observed up to a concentration of 15.3 mg/L. No additional data were reported.
Reference:	Huels AG (1988). Biology - Toxicology, Report No. A 126 (July 27).
Reliability:	Medium because a scientifically defensible or guideline method was used; however, limited study information was available.

From ECOSAR Model

Type:	**96-hour EC_{50}**

Species:	Green algae
Value:	105 mg/L
Method:	Modeled, ECOSAR (using log Kow of 3.18)
GLP:	Not Applicable
Test Substance:	DDDA
Results:	No additional data.
Reference:	Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210 (submitted for publication).
Reliability:	Estimated value based on accepted model.

Additional References for Acute Toxicity to Aquatic Plants: None Found.

5.0 Mammalian Toxicity

5.1 Acute Toxicity

Type:	**Oral LD_{50}**
Species/Strain:	Rat/Strain not specified
Value:	> 3000 mg/kg
Method:	The procedures used in the test were based on the recommendations of the following guideline: OECD Guideline 401 "Acute Oral Toxicity." 3000 mg/kg of the substance in corn oil was given to 5 rats/sex.
GLP:	Unknown
Test Substance:	Dodecanedioic acid, purity not reported
Results:	No animals died during the study. No animal showed any pathological changes when submitted to necropsy 14 days after dosing. No other details were presented.
Reference:	Huels (1988). Report No. ADW 170 (cited in IUCLID (2000). IUCLID Dataset, "Dodecandioic acid" (February 19)).
Reliability:	Medium because a scientifically defensible or guideline method was used; however, limited study information was available.

Type:	**Oral ALD**

Species/Strain:	Rats/ChR-CD
Value:	> 17,000 mg/kg
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. The test material was administered by intragastric intubation in single doses as a suspension in peanut oil to young adult male rats. Dose levels of 2250, 5000, 7500, 11,000, and 17,000 mg/kg were tested. Clinical signs and body weights were evaluated throughout the test. Survivors were sacrificed 14 days later and pathological evaluations were conducted.
GLP:	No
Test Substance:	Dodecanedioic acid, purity 99+%
Results:	No animals died during the study. Weight loss for 1 day after dosing was noted at 5000 mg/kg and above. No clinical signs were reported. Histopathological results indicated that no lesions attributable to the administration of the test compound were observed.
Reference:	DuPont Co. (1964). Unpublished Data, Haskell Laboratory Report 51-64, "Acute Oral Test" (May 22).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Acute Oral Toxicity:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Huels AG (1989). Biology - Toxicology, Report No. 1465 (March 21).

Proctor & Gamble Co. (1986). Hazelton Laboratories Inc. Study No. 50507616 (January 22) (cited in TSCA Fiche OTS0537648).

Proctor & Gamble Co. (1985). Hazelton Laboratories Inc. Study No. 50507615 (December 6) (cited in TSCA Fiche OTS0542098).

Type:	**Acute Inhalation ALC**
Species/Strain:	Rats/Strain not specified
Value:	> 4.3 mg/L
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

	Groups of 6 rats were given single 4-hour exposures, nose only, to dodecanedioic acid dust at concentrations of 0.81 and 4.3 mg/L. The rats were weighed and observed daily (weekends excluded) over a 14-day recovery period. Necropsy examinations were not conducted.
GLP:	No
Test Substance:	Dodecanedioic acid, purity 98+%
Results:	Aerosol particle sizes (MMADs) were 3.6 μm in the 0.81 mg/L experiment and 4.3 μm in the 4.3 mg/L experiment. Clinical signs observed in rats immediately after exposure were red ocular and nasal discharge, signs frequently seen in animals being restrained. Rats showed dose-related transient weight losses for one day after exposure, followed by resumption of a normal weight gain rate. No mortality was observed in this study.
Reference:	DuPont Co. (1994). Unpublished Data, Haskell Laboratory "ALC Test" (August 5).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Acute Inhalation Toxicity: None Found.

Type:	**Dermal LD_{50}**
Species/Strain:	Male rabbits/Albino
Exposure Time:	24 hours
Value:	> 6000 mg/kg
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. Six male rabbits weighing between 2.9 and 3.2 kg were clipped free of hair over the trunk area and fitted with plastic collars. Doses of 6000 mg/kg of test material, moistened with physiological saline, were applied to the back of each rabbit under gauze pads. The trunk of each rabbit was then wrapped with a layer of plastic wrap, gauze bandage and adhesive bandage. After a 24-hour exposure, the wrappings were removed and the treated site was washed with water and dried. The rabbits were observed and weighed over a 14-day recovery period and then sacrificed. Necropsy examinations were not performed.
GLP:	No
Test Substance:	Dodecanedioic acid, purity 100%

Results:	No deaths occurred during the study. Slight skin irritation, diarrhea, and nasal discharge were observed. Two rabbits had weight loss on the day after dosing and there was sporadic weight loss 3-13 days after dosing.
Reference:	DuPont Co. (1980). Unpublished Data, Haskell Laboratory Report 921-80, "Acute Skin Absorption Test on Rabbits – LD_{50}" (December 4).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Acute Dermal Toxicity: None Found.

Type:	**Dermal Irritation**
Species/Strain:	Male rabbits/Albino
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. Six male albino rabbits were clipped free of hair on the trunk and lateral areas and placed in stocks. Doses of 0.5 g of powder as supplied were applied to intact skin under gauze squares. Rubber sheeting was then loosely wrapped around the trunk and secured with adhesive tape. After 24 hours, the rabbits were removed from the stocks, the patches taken off, and the reactions observed. Observations were also made at 48 hours and graded according to the system of the regulations of the Federal Hazardous Substances Act (FR 1975 Section 1500.41).
GLP:	No
Test Substance:	Dodecanedioic acid, purity 100%
Results:	No skin irritation was observed at any time during this test.
Reference:	DuPont Co. (1976). Unpublished Data, Haskell Laboratory Report 344-76, "Skin Irritation Test on Rabbits" (May 7).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional Reference for Dermal Irritation:

Data from this additional source support the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

Huels AG (1989). Biology - Toxicology, Report No. 1466 (February 28) (cited in IUCLID (2000). IUCLID Dataset, "Dodecandioic acid" (February 19)).

Type:	**Dermal Sensitization**
Species/Strain:	Female guinea pigs/Strain not specified
Method:	The procedures used in the test were based on the recommendations of the following guideline: OECD Guideline 406 "Skin Sensitization." Twenty female guinea pigs were administered dodecanedioic acid intracutaneously at 0.5% or epidermally at 25 and 50%. No other details were presented.
GLP:	No
Test Substance:	Dodecanedioic acid, purity not reported
Results:	No sensitization reactions were observed 24 or 48 hours after the patch test.
Reference:	Huels AG (1989). Biology - Toxicology, Report No. 1468 (March 21) (cited in IUCLID (2000). IUCLID Dataset, "Dodecandioic acid" (February 19)).
Reliability:	Medium because a scientifically defensible or guideline method was used; however, limited study information was available.

Additional References for Dermal Sensitization: None Found.

Type:	**Eye Irritation**
Species/Strain:	Rabbits/Albino
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. 0.1 mL of solid test material was placed into the right conjunctival sac of each of 2 albino rabbits. Twenty seconds after contact, one treated eye was washed with tap water for 1 minute. The treated eye of the other rabbit was not washed. Observations of the cornea, iris, and conjunctiva were made with a hand-slit lamp at 1 and 4 hours and at 1, 2, and 3 days. A biomicroscope and fluorescein stain were used at examinations the day after treatment.
GLP:	No
Test Substance:	Dodecanedioic acid, purity 100%
Results:	The test substance produced a small area of slight corneal opacity and mild conjunctival irritation with no significant iritic effect in a rabbit eye that was not washed after dosing. Corneal opacity was reversible, and the eye was normal within 7 days. An eye dosed with the compound and

	promptly washed had transient, mild conjunctival irritation with no corneal or iritic effect, and was normal within 2 days.
Reference:	DuPont Co. (1976). Unpublished Data, Haskell Laboratory Report 316-76, "Eye Irritation Test in Rabbits" (April 30).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional Reference for Eye Irritation:

Data from this additional source support the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

Huels AG (1989). Biology - Toxicology, Report No. 1467 (July 10) (cited in IUCLID (2000). IUCLID Dataset, "Dodecandioic acid" (February 19)).

5.2 Repeated Dose Toxicity:

Type:	**10-Dose Subacute Oral**
Species/Strain:	Rats/Chr:CD
Sex/Number:	Male/6
Exposure Period:	10 days
Frequency of Treatment:	5 times/week for 2 weeks
Exposure Levels:	0 and 5000 mg/kg
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. Rats were administered the test substance by intragastric intubation as a suspension in peanut oil. Groups of 3 test and 3 control rats were sacrificed 4 hours and 14 days after the last treatment. Clinical signs and body weights were recorded throughout the test. Pathological examinations were conducted on all rats.
GLP:	No
Test Substance:	Dodecanedioic acid, purity 99+%
Results:	No mortality occurred during the study. Toxic signs during the 1st week included weight loss after the 1st dose and inactivity. During the 2nd week, weight loss was recorded after the 6th dose. During the recovery period, weight gain slightly greater than the controls was observed. No cumulative toxicity or histopathological lesions were seen.

Reference:	DuPont Co. (1964). Unpublished Data, Haskell Laboratory Report No. 51-64, "Ten-Dose Subacute Oral Test" (May 22).
Reliability:	High because a scientifically defensible or guideline method was used.
Type:	**Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test**
Species/Strain:	Rat/Crl:CD®BR
Sex/Number:	Male and female/12 per sex per dose group
Route of Exposure:	Oral
Exposure Period:	14 days premating through 4-day lactation period (approximately 50 days)
Frequency of Treatment:	Daily
Exposure Levels:	0, 100, 500, 1000 mg/kg
Method:	The procedures used in the test were based on the recommendations of the following guideline:

OECD Guideline 422.

Male and female rats (approximately 71 days old at the initiation of dosing) were administered an oral, daily dose of 0, 100, 500, or 1000 mg/kg/day dodecanedioic acid. After 14 days of dosing, the rats were bred within their respective treatment groups and allowed to produce litters. The test substance was administered continuously to male and female rats during breeding, gestation, and lactation. Formulations of the dodecanedioic acid in 0.5% methyl cellulose were prepared daily, for use on the same day. Twice during the study, samples were collected from each dose level to evaluate concentration and/or stability.

Body weights and food consumption for males and females were recorded weekly during the premating period. Females were weighed periodically throughout gestation and lactation, and males were weighed weekly. Food consumption was assessed for the P_1 mating pairs during the cohabitation period. Weekly food consumption measurements resumed for the P_1 males at the end of the cohabitation period and continued for the remainder of the study. Food consumption of pregnant females was recorded periodically throughout the gestation and lactation period. Clinical signs were recorded weekly throughout the entire study.

Blood samples were collected from the male rats at the end

of the study for hematological and clinical chemical measurements. Nine hematologic parameters and 16 clinical chemistry parameters were measured or calculated.

After litter production, all adult rats were sacrificed for gross pathological evaluation. The liver, kidney, adrenals, brain, heart, spleen, testes, and ovaries were collected for histopathological examination. Organ weights were collected for the liver, kidney, thymus, testes, and epididymides.

Additional details for reproductive and pup/weanling information can be found in Section 5.4.

Body weights, body weight gains, food consumption, organ weights, and clinical laboratory data were analyzed by a one-way analysis of variance. When the test for differences among test groups means was significant, pairwise comparisons between control and test groups were made with the Dunnett's test. The Bartlett's test for homogeneity of variances was performed on the organ weight and clinical laboratory data and, when significant, was followed by nonparametric procedures.

The incidence of clinical observations was evaluated by the Fisher's Exact test with a Bonferroni correction and if significant, was followed by the Cochran-Armitage test for trend.

GLP: Yes

Test Substance: Dodecanedioic acid, purity 100%

Results: Analysis of test substance indicated that the test substance concentrations were at the targeted level. The stability results indicated that the test substance was stable at all concentrations under the conditions of the study.

There were no mortalities during the study. Dodecanedioic acid did not significantly affect the overall body weights, body weight gains, food consumption, or food efficiency in male or female rats. There were no significant differences in incidence of clinical observations during the study; however, some isolated, transient cases of hypoactivity were observed shortly after dosing in the 500 and 1000 mg/kg male rats and the 1000 mg/kg female rats.

There were no significant differences between the control and treated rats with respect to the reproductive performance

of male or female rats. Additional details for the reproductive toxicity subset can be found in Section 5.4.

The mean total leukocyte counts were decreased in male rats treated with 500 and 1000 mg/kg dodecanedioic acid; however, the decreases in the 500 mg/kg group were not significantly different. The decreases in total leukocyte count were attributable to decreases in lymphocyte counts, which were significant in the 500 and 1000 mg/kg groups. The absence of both morphological alterations in the spleen and decreases in thymus weights, and normal serum globulin concentrations suggest that the immunological impact was minimal. There were no compound-related effects on the mean final body weights, or organ weights, nor were there any gross or microscopic changes noted that were attributable to the test substance.

The no-observed-adverse-effect level (NOAEL) was 1000 mg/kg/day. The dose level at which no effects were produced was 100 mg/kg for male rats and 500 mg/kg for female rats.

Reference: DuPont Co. (1992). Unpublished Data, Haskell Laboratory Report No. 229-92, "Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test" (June 9).

Reliability: High because a scientifically defensible or guideline method was used.

Additional References for Repeated Dose Toxicity: None Found.

5.3 Developmental Toxicity

Species/Strain:	Rat/Crl:CD®BR
Sex/Number:	Male and female/12 per sex per dose group
Route of Administration:	Gavage
Exposure Period:	14 days premating through 4-day lactation period (approximately 50 days)
Frequency of Treatment:	Daily
Exposure Levels:	0, 100, 500, 1000 mg/kg
Method:	The procedures used in the test were based on the recommendations of the following guideline:

OECD Guideline 422.

Details for the subchronic portion, including dosing scheme, toxicological parameters studied, and statistical analyses can be found in Section 5.2.

Following the 14-day premating period, each female was continually housed with a randomly selected male of the same dosage group until evidence of copulation was obtained (intravaginal or extruded copulation plug, or presence of sperm in vaginal smear) or until 2 weeks elapsed.

Live and dead pups in each litter were counted as soon as possible after delivery was complete. On the day when delivery was complete (lactation day 0), pups in each litter were counted and weighed collectively by sex. On days 0 and 4, offspring were individually handled and examined for abnormal behavior and/or appearance. Any dead, missing, or abnormal pups were recorded at each examination period. On day 4 postpartum, pup counts, weights, and external appearance were assessed and the litters were sacrificed and discarded without pathological evaluation. Other reproductive parameters recorded or calculated included mating, fertility and gestation indices, corpora lutea, and implantation site data.

Gestation length was analyzed by a one-way analysis of variance. When the test for differences among test group means was significant, pairwise comparisons between control and test groups were made with the Dunnett's test. Measures of reproduction and lactation performance were evaluated with either the Fisher's Exact test (mating, fertility, and gestation indices and litter survival) or the Kruskal-Wallis test (pup number, survival, weights, viability index, and lactation index). Sequential trend testing was applied to the corpora lutea and implantation side data, using Jonckheere's test.

GLP: Yes

Test Substance: Dodecanedioic acid, purity 100%

Results: Results of the subchronic portion of the study, including effects on body weights, food consumption, clinical signs of toxicity, clinical chemistry, and pathology/histopathology, can be found in Section 5.2. Results of reproductive performance are detailed below.

There were no significant differences between the control and treated rats with respect to the reproductive performance of male or female rats, which included number of corpora

lutea, number of implantation sites, sex ratio, and mean fetal weight.

There were no test substance-related effects on clinical observations in pups or pup body weights.

Pregnancy ratios were 11/12, 10/12, 10/11, and 11/12 for the 0, 100, 500, and 1000 mg/kg groups, respectively. A summary of other reproductive outcomes (means/litter) are provided in the table below:

Concentration (mg/kg)	0	100	500	1000
Corpora Lutea:	19.6	18.0	19.6	20.2
Implantations:	17.2	17.5	18.5	16.8
Total No. of Resorptions:	NR	NR	NR	NR
Total No. of Fetuses:	15.2	15.6	16.4	15.5
Total No. of Live Fetuses:	15.2	14.6	16.2	15.5
Mean Fetal Weight (g):	6.7	6.6	6.5	6.5
Sex Ratio (male/female):	0.51	0.51	0.48	0.47
NR = Not Reported				

The no-observed-adverse-effect level (NOAEL) was 1000 mg/kg/day.

Reference: DuPont Co. (1992). Unpublished Data, Haskell Laboratory Report No. 229-92, "Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test" (June 9).

Reliability: High because a scientifically defensible or guideline method was used.

Additional References for Developmental Toxicity: None Found.

5.4 Reproductive Toxicity

Species/Strain: Rat/Crl:CD®BR
Sex/Number: Male and female/12 per sex per dose group
Route of Administration: Gavage
Exposure Period: 14 days premating through 4-day lactation period

	(approximately 50 days)
Frequency of Treatment:	Daily
Exposure Levels:	0, 100, 500, 1000 mg/kg
Method:	The procedures used in the test were based on the recommendations of the following guideline: OECD Guideline 422. Details for the subchronic portion, including dosing scheme, toxicological parameters studied, and statistical analyses can be found in Section 5.2. Following the 14-day premating period, each female was continually housed with a randomly selected male of the same dosage group until evidence of copulation was obtained (intravaginal or extruded copulation plug, or presence of sperm in vaginal smear) or until 2 weeks elapsed. Live and dead pups in each litter were counted as soon as possible after delivery was complete. On the day when delivery was complete (lactation day 0), pups in each litter were counted and weighed collectively by sex. On days 0 and 4, offspring were individually handled and examined for abnormal behavior and/or appearance. Any dead, missing, or abnormal pups were recorded at each examination period. On day 4 postpartum, pup counts, weights, and external appearance were assessed and the litters were sacrificed and discarded without pathological evaluation. Other reproductive parameters recorded or calculated included mating, fertility and gestation indices, corpora lutea, and implantation site data. Gestation length was analyzed by a one-way analysis of variance. When the test for differences among test groups means was significant, pairwise comparisons between control and test groups were made with the Dunnett's test. Measures of reproduction and lactation performance were evaluated with either the Fisher's Exact test (mating, fertility, gestation index, and litter survival) or the Kruskal-Wallis test (pup number, survival, weights, viability index, and lactation index). Sequential trend testing was applied to the corpora lutea and implantation side data using Jonckheere's test.
GLP:	Yes
Test Substance:	Dodecanedioic acid, purity 100%

Results:

Results of the subchronic portion of the study, including effects on body weights, food consumption, clinical signs of toxicity, clinical chemistry, and pathology/histopathology, can be found in Section 5.2. Results of reproductive performance are detailed below.

There were no significant differences between the control and treated rats with respect to the reproductive performance of male or female rats which included mating index and fertility indices, gestation length, number of implantation sites, sex ratio, gestation ratio, percentage of pups born alive, and number of pups surviving to day 4 of lactation.

There were no test substance-related effects on clinical observations in pups or pup body weights.

A summary of reproductive outcomes are provided in the table below:

Dose (mg/kg)	0	100	500	1000
Mating Index (%):	100.0	100.0	91.7	100.0
Fertility Index (%):	91.7	83.3	90.9	91.7
Gestation Length (days):	22.3	22.2	22.2	22.4
Implantations (mean/litter):	17.2	17.5	18.5	16.8
Implantation efficiency (%):	NR	NR	NR	NR
Gestation Index:	100.0	100.0	100.0	100.0
Mean % Born Alive:	100.0	95.0	98.7	100.0
0-4 Day Viability (%):	99.4	98.2	97.3	98.8
Sex Ratio (male/female):	0.51	0.51	0.48	0.47
NR = Not Reported				

The no-observed-adverse-effect level (NOAEL) was 1000 mg/kg/day.

Reference:

DuPont Co. (1992). Unpublished Data, Haskell Laboratory Report No. 229-92, "Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test"

	(June 9).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Reproductive Toxicity: None Found.

5.5 Genetic Toxicity

Type:	***In vitro* Bacterial Reverse Mutation Assay**
Tester Strain:	*Salmonella typhimurium* TA98, TA100, TA1535, TA1537, and TA1538
Exogenous Metabolic Activation:	With and without Luminal-induced rat liver S9
Exposure Concentrations:	10 to 5000 µg/plate
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. The method was reported as following Ames et al. (1975). Mutat. Res., 31:347-364. The test substance was checked for possible mutagenic activity, using the Ames I mutagenicity test. Test organisms were five histidine-auxotrophic (his +) strains of *Salmonella*. Substance concentrations of 10 to 5000 µg/plate were tested (Petri dishes with nutrient media). Substances that have no mutagenic effect at a concentration of 5000 µg/plate may be designated as non-mutagenic in the Ames I classification. Two tests were conducted. The solvent used in the test was dimethyl sulfoxide. Positive controls included the following: aminoanthracene, nitrofluorene, and sodium azide. No other details were presented.
GLP:	Unknown
Test Substance:	Dodecanedioic acid, purity not reported
Results:	Negative
Remarks:	The test substance was non-mutagenic versus all test strains, with and without metabolic activation, and using a pre-incubation test, even with addition of 5000 µg/plate. Toxicity occurred at 500 µg/plate and above.
Reference:	Huels AG (1989). Biology - Toxicology, Report No. 88/69 (July 27) (cited in IUCLID (2000). IUCLID Dataset, "Dodecandioic acid" (February 19)).

Reliability: Medium because a scientifically defensible method was used; however, only limited study information was available.

Additional Reference for *In vitro* Bacterial Reverse Mutation Assay:

Data from this additional source support the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

Huels (1989). Unpublished report 80/16 (cited in IUCLID (2000). IUCLID Dataset, "Dodecandioic acid" (February 19)).

Type: ***In vitro* Clastogenicity Studies:** No Data.

Type:	***In vivo* Mouse Micronucleus Assay**
Species/Strain:	Mouse/Crl:CD®-1(ICR)BR
Sex/Number:	Male and female/10 per sex per concentration
Route of Administration:	Oral gavage
Concentrations:	0, 1000, 2000, or 5000 mg/kg (administered twice)
Method:	The procedures used in the test were based on the recommendations of the following guidelines:

EPA Guideline published in 40 CFR 798.5395.

OECD Draft Guideline 474.

Dodecanedioic acid (DDDA) was tested in male and female mice to determine its ability to induce micronuclei in bone marrow polychromatic erythrocytes (PCEs). Doses of 0 (control), 1000, 2000, or 5000 mg/kg body weight were administered twice, approximately 24 hours apart, by oral intubation. Animals were 55 days of age at the start of the test. Male mice weighed 27.6-34.0 grams and female mice weighed 22.6-28.2 grams. Groups of 5 male and 5 female mice from the negative control and DDDA-treated groups were sacrificed 24 and 48 hours after the final dosing. The positive control indicator group of 5 male and 5 female mice was concurrently treated with cyclophospahmide (CP) doses of 20 mg/kg on 2 consecutive days and sacrificed 24 hours after the 2nd dose. Animals were housed individually in standard wire mesh cages. Room temperature was maintained at 23±2°C with a relative humidity of 50±10%.

Dosing suspensions were prepared immediately prior to use on each day. DDDA was prepared in 0.5% methyl cellulose

at concentrations of 66.67, 133.33, and 333.33 mg/mL. The treatments were administered by oral intubation in a volume of 15 mL/kg, yielding effective doses of 1000, 2000, and 5000 mg/kg. The vehicle was similarly administered to the negative control group. Cyclophosphamide (CP) was the positive indicator.

Each animal was observed for clinical signs approximately 3-5 hours post-dosing and daily thereafter. Body weights were recorded prior to dosing and prior to sacrifice. The animals were sacrificed 24 and 48 hours after the final dosing. Both femora were removed, aspirated, and flushed into fetal bovine serum. The marrow button was collected by centrifugation. Most of the supernatant was removed, and the cells were resuspended in the remaining serum. An automatic blood smearing instrument was used to make the bone marrow smears. At least 2 slides per animal were prepared and fixed in absolute methanol. The slides were stained with acridine orange.

One thousand polychromatic erythrocytes (PCEs) were evaluated for each animal. The number of cells with micronuclei (MNPCEs) was recorded. In addition, the ratio of polychromatic to normochromatic erythrocytes (NCEs) was determined. All bone marrow smears were coded to ensure that the group to which they belonged was unknown to the investigator.

Data for percent micronucleated PCEs (MN-PCEs) and proportion of PCEs among 1000 erythrocytes were transformed prior to analysis using the arcsine square-root function. Data from each sex and sacrifice time were analyzed separately by a one-way analysis of variance (ANOVA). If the ANOVA was significant, individual dose groups were compared to the negative control using Dunnett's test. The positive control group was not included in the analyses for effects of the test compound. All analyses were one-tailed.

The concentration levels were selected on the basis of a preliminary study in which administration of 1250, 2500, and 5000 mg/kg produced no adverse effects.

GLP: Yes
Test Substance: Dodecanedioic acid, purity 100%
Results: Negative
Remarks: No significant changes in body weight were observed in any

DDDA-treated group at the time of sacrifice. Several animals within the negative control group and each DDDA-treated group exhibited ruffled fur either immediately prior to dosing, 3-5 hours post-dosing, or the day following the last dose.

No statistically significant increases in the frequency of micronucleated PCEs were found in DDDA-treated animals at any sampling time. Also, no significant decrease in the ratio of young PCEs to mature normochromatic erythrocytes was observed. Under study conditions, DDDA did not induce micronuclei.

Reference: DuPont Co. (1992). Unpublished Data, Haskell Laboratory Report No. 379-92, "Mouse Bone Marrow Micronucleus

Reliability: High because a scientifically defensible and guideline method was used.

Additional References for *In vivo* Genetic Toxicity: None Found.